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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/507,272	11/22/2004	Domenico Maglione	10500-008	4002

29391 7590 10/20/2005

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EXAMINER	
TSAY, MARSHA M	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 10/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/507,272	MAGLIONE ET AL.	
	Examiner	Art Unit	
	Marsha M. Tsay	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *23-29* is/are allowed.

6)☒ Claim(s) *16-22 and 30-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

This Office Action is in response to Applicants' amendment received on August 17, 2005. Claims 16-35 are pending and currently under examination.

Priority: Priority date is March 5, 2002.

Withdrawal of Objections and Rejections

The objection to claims 16, 23, 35 because of minor informalities is withdrawn.

The rejection of claims 23-26, 28-35 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn.

The rejection of claims 16-22, 27, 30-35 under 35 U.S.C. 102(b) as being anticipated by Ziche et al. (1997 Lab. Invest. 76(4): 517-531) is withdrawn.

New Objections and Rejections

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 16-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ziche et al. (1997 Laboratory Investigation 76(4): 517-531) and further in view of Failla et al. (2000 J. Invest. Dermatology 115(3): 388-395).

Ziche et al. (1997 Laboratory Investigation 76(4): 517-531) teach the preparation and purification of recombinant PLGF-1 for inducing rabbit corneal neovascularization *in*

vivo (p. 518). Placental Growth Factor-1 was assayed for angiogenic activity in the rabbit cornea and promoted angiogenesis in the avascular rabbit cornea (p. 518). While Ziche et al. teach promotion of angiogenesis with PLGF-1, Ziche et al. do not teach the application of PLGF-1 in the treatment of a state selected from the group consisting of diseases involving cutaneous or subcutaneous connective tissue, scleroderma, and early skin aging due to exposure to atmospheric aggressive agents.

Failla et al. (2000 J. Invest. Derm. 115(3): 388-395) teach PLGF-1 is induced in human keratinocytes during wound healing. Fallia et al. teach PLGF-1 is expressed *in vivo* by migrating keratinocytes at the wound site (p. 391). The involvement of PLGF in wound healing was tested by analyzing its expression in human full-thickness wounds *in vivo* (p. 391). Failla et al. teach their data demonstrate that keratinocytes are a source of PLGF during wound healing *in vivo* and indicate a role for PLGF-1 in the neoangiogenesis process associated with cutaneous wound repair (p. 388, abstract).

It would have been obvious to a person having ordinary skill in the art to formulate a composition comprising PLGF-1 (Ziche et al.) and use it in promoting angiogenesis in the treatment of a pathological alteration involving skin tissue (claims 16-22) because Failla et al. teach and suggest a role for PLGF-1 in the neoangiogenesis process associated with cutaneous wound repair.

Claims 30-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carmeliet et al. (WO 0156593). Carmeliet et al. teach enhanced revascularization of acute myocardial infarcts by administration of PLGF-1 (p. 17). In working example 3,

Carmeliet et al. show the treatment of infarcted mice with PLGF dimer with different dosage units of 715 ng/day and 3.5 ug/day, respectively (p. 18, line 10). Carmeliet et al. also disclose dosages of PLGF composition that can be administered. For example, examples of therapeutically effective amounts of PLGF composition are preferably an amount of about 2 to 2,000 ug per kg of body weight of mammal to be treated. Therefore, depending on the body weight of the subject to be treated, the amount of PLGF-1 administered can vary. On pages 10-13, Carmeliet et al. also disclose various suitable pharmaceutical carriers, surfactants, and agents that can be used to formulate various forms of PLGF-1 compositions, such as solutions, emulsions, pellets, and powders. Carmeliet et al. do not teach PLGF-1 to be in a composition in an amount from 50 ug to 30 mg per unitary dose for parenteral use and/or in an amount from 0.1 mg to 10 mg per gram for topical use.

It would have been obvious to a person having ordinary skill in the art to formulate a composition comprising PLGF-1 as an active principle in dimeric form, and in an amount of about 2 to 2,000 ug per kg of body weight of subject (claims 30-35) with a suitable pharmaceutical carrier and/or agent because Carmeliet et al. teach and suggest the use of compositions comprising PLGF-1 dimer as active principle for improving infarct angiogenesis and arteriogenesis.

Claims 23-29 are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marsha M. Tsay whose telephone number is 571-272-2938. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen Cochrane Carlson PhD

October 9, 2005

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER